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NEW DEVELOPMENTS IN BIOTECHNOLOGY: U.S. INVESTMENT IN BIOTECHNOLOGY

Contractor Reports, Part 2

Collaborative Research Relationships in Biotechnology

December 1987

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COLLABORATIVE RESEARCH RELATIONSHIPS IN BIOTECHNOLOGY

Final Report

Submitted to:

Biological Applications Program
Office of Technology Assessment
United States Congress

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Overview of the Study

Introduction

The joint involvement of individuals and institutions from different sectors in the funding, performance, and utilization of scientific work is by no means a new phenomenon. Yet the rapid proliferation of collaborative research relationships in recent years -- partnerships between universities, industry, and government -- has greatly extended the frequency, scope, and visibility of such activities. Paralleling this growth in collaborative research relationships is an increasing interest on the part of both policymakers and researchers alike in:

- Categorizing the diversity of forms these relationships has taken.
- Understanding the effects of these new partnerships on the institutions and individuals involved, on the U.S. research agenda, and on the pace of commercialization in a wide variety of technical areas.
- Assessing the potential problems, benefits, and outcomes resulting from such collaborations.

Early concerns about collaborative research arrangements, particularly those involving universities and industry, were focused primarily on issues of academic freedom, proprietary information, patent rights, and other potential conflicts of interest among collaborating partners. As these research arrangements have evolved, and our experience base has grown, some of the most obvious difficulties have been resolved. However, many of the early concerns now have been replaced by more complex, and perhaps more subtle, questions about these new partnerships. How effective have these arrangements been in

meeting the needs of participating institutions? What effects have collaborative relationships had on the nation's R&D agenda? How have collaborative arrangements affected academic research and the role of the university? Have these new partnerships stimulated technological innovation and improved America's industrial competitiveness?

Study Scope

This report reviews and summarizes what is known about collaborative research arrangements in biotechnology and analyzes the structure, scope, and potential problems, benefits, and outcomes of such collaborative activities. The primary focus of the study is on U.S. university-industry research collaborations. For the purposes of this study, collaborative research includes: institutional-institutional arrangements (such as those between a university and a corporation or firm, or those between a number of industrial partners and one or more universities -- often with state and/or Federal involvement) and individual-institutional arrangements (such as those between an academic scientist and a biotechnology company).

In order to understand and assess a variety of collaborative research relationships in biotechnology outside the domestic university-industry context, this study also briefly explores U.S. industry-industry research collaborations, to the extent that they exist in this country, and collaborative arrangements between foreign companies and U.S. firms, universities, and academic researchers.

The literature on university-industry research arrangements in biotechnology presents two vastly different and opposing viewpoints on the potential problems, benefits, and outcomes of collaboration. Although few proponents of either view espouse the degree of polarity presented below, these two poles of a continuum can be characterized as:

- **The Negative Pole:** The influx of commercial interests on campus has perverted the fundamental structure and values of the university, distorted academic research agendas, and adversely affected everything from scientific freedom and communication, to basic professorial responsibilities, including the teaching and training of students.
- **The Positive Pole:** University-industry research collaboration is the critical key to enhancing our nation's industrial competitiveness, productivity, and innovation, and that such arrangements will facilitate critically needed technology transfer and result in sustained economic development, job retention, and job creation.

Many assumptions are made on both sides of the issue. Often the only "evidence" offered by researchers to substantiate their claims is anecdotal, in lieu of hard facts or data. Therefore, this study weighs the opposing views, and attempts to distinguish the rhetoric from the reality.

Study Issues and Questions

The study addresses the following issues and questions:

- Trends in University-Industry Research Arrangements
  - What major factors have made collaborative research in biotechnology so attractive to universities, industry, and individual scientists?
  - Is the trend toward university-industry collaboration in biotechnology expected to continue?
- Types of Collaborative Research Arrangements

- What types of collaborative research arrangements exist in biotechnology between universities and industry?

- How are collaborative research arrangements in biotechnology similar to, or different than, research partnerships in other fields?

- Potential Benefits of University-Industry Research Collaborations in Biotechnology

  - What are the major benefits of research collaboration in biotechnology?

  - Do the benefits differ for:
    . universities?
    . industry?
    . individual scientists?
    . students?
    . U.S. industrial competitiveness?

- Potential Problems of University-Industry Research Collaborations in Biotechnology

  - What are the major problems of research collaboration in biotechnology?

  - Do the problems differ for:
    . universities?
    . industry?
    . individual scientists?
    . students?

- Variations in The Benefits and Problems of University-Industry Research Collaborations in Biotechnology

  - Do the benefits and problems vary by the type of collaborative arrangement?

  - Do the benefits and problems vary by the sector or area of research (e.g., agriculture; chemicals; pharmaceuticals)?

  - Do the benefits and problems vary by the size of the collaborating industrial partner?

  - How do universities vary in their responses to the benefit and problems presented by collaborative research arrangements?

- Foreign Company Research Collaborations with the U.S. in Biotechnology

  - What information exists concerning collaborations between foreign companies and U.S. universities, or U.S. academic researchers?

- What information exists concerning collaborations between foreign companies and U.S. industry?

- U.S. Industrial Research Collaborations In Biotechnology
  - What information exists concerning domestic industry-industry collaborations?
  - What is the frequency and pattern of U.S. industrial collaborations?
- Recommendations and Policy Issues
  - What can be done to improve the process or the outcomes of collaborative research in biotechnology?
  - What additional areas or topics are in need of further study?

Study Design

The study was completed in two phases. Phase One consisted of a detailed review and analysis of the literature on collaborative research arrangements in biotechnology -- with a particular focus on books, Congressional hearings, articles, and monographs that discussed university-industry research collaborations. Examples of primary source material are listed in Appendix A.

Phase Two consisted of a series of in-depth interviews with the primary investigators whose research and publications on university-industry research relationships in biotechnology was reviewed in Phase One. For a list of participants, see Appendix B. All interviews were conducted by telephone.

Chapter 1

Trends in University-Industry Research Arrangements

Introduction

Although the issues associated with the commercialization of university research have recently received a great deal of public attention, partnerships between academia and business are not new. Industry and the academic community have long recognized that they share many mutual research interests and historically have sought ways to capitalize on those interests (Johnson, 1982). Many researchers and practitioners have chronicled the historical antecedents of the trend toward university-industry collaborations in a variety of disciplines (Government-University-Industry Research Roundtable, 1986; Etzkowitz, 1983; Kenney, 1986; Tornatzky, Solomon, and Eveland, 1987). Our concerns here are more recent: What has caused the current surge of new arrangements among universities and industry?

Recent Factors that Stimulated University-Industry Collaboration

During the 1970s, several key factors in the university environment converged to stimulate increasing interest on the part of academic faculty and university administrators in seeking "non-traditional" sources of funding. First, there was a growing awareness that in many fields, the costs of doing research was exceeding the institution's capacities to pay for research from traditional sources -- government funding, university budgets, and private foundations (Roundtable, 1986). Such cost increases have been especially prevalent in fields that require large-scale, technologically advanced

equipment and instruments and, consequently, the involvement of larger numbers of assistants with diverse skills (Etzkowitz, 1983). Second, increasing Federal budget deficits, soaring inflation, and the election of President Reagan in November, 1980 signaled the possibility of some changes in Federal support for university research which many scientists and university administrators feared would result in drastically cut budgets for all scientific research (Roundtable, 1986; Kennedy, 1985).

During this same time period, American industry was becoming increasingly aware that its traditional position of "technological supremacy" was being challenged on a variety of fronts, and that its competitive edge in many sectors was in jeopardy (Business Higher-Education Forum, 1983; President's Commission on Industrial Competitiveness, 1985; Solomon and Tornatzky, 1986). Since there was a growing consenus that competitiveness was linked to innovation, and that university research and technology transfer played a critical role in our nation's ability to compete, business began to show greater interest in creating and strengthening its own connections with the academic community (Gray, Solomon, and Hetzner, 1986).

The relative decline of U.S. industrial competitiveness and productivity soon became a topic of intense public concern, affecting Federal, state, and local politics (Roundtable, 1986). The presumption that strengthening the links between industry and university research could improve America's economic malaise, gave impetus to a variety of new government policy initiatives over the last decade (Peters and Fusfeld, 1981; Prager and Omenn, 1980). These included:

- The Patent and Trademark Amendments of 1980 which included changes in Federal patent laws relating to universities. (Patent and Trademark Amendments Act, P.L. 96-517, 1980).
- The Stevenson-Wydler Technology Innovation Act of 1980 to promote cooperative research and technology transfer.
- The 1981 Economic Recovery Tax Act (ERTA) which included tax incertives for R&D.
- Relaxation of antitrust regulations, in part to facilitate research collaborations among previously competitive industrial firms.
- Federal funding for university-industry cooperative programs and projects, for example through the National Science Foundation.
- Growth of state economic development programs that provide incentives to promote university-industry cooperation.

(Association of American Universities, 1986; Ruscio, 1984).

Trends in University-Industry Research in Biotechnology

This confluence of events and policies clearly increased the interest of universities, industry, and government in activities pertaining to partnerships between academia and business in all fields of science. However, because of the relatively controversial nature of biotechnology, the potential impact of resulting products and processes on a diversity of industrial sectors, a multitude of existing and newly proposed federal and state funding initiatives in this area, and an unprecedented influx of investment capital, interest in collaborative research relationships in biotechnology has been especially keen.

Interviewees were asked whether they expected this trend toward university-industry research collaborations in biotechnology to continue. All the respondents felt the trend toward academic and business partnerships would

continue -- "the pattern of industry-university collaboration is engrained now" (Martin Kenney, personal communication). However, there was no consensus on whether the growth rate will maintain the same kind of pace we have witnessed in recent years. As Blumenthal points out, the natural history of technological breakthroughs is "a few years of intense collaboration, after which, things usually settle down". However, he is not at all sure that things will ever settle down in biotechnology. In part, the rate of future growth will depend on some decisions that have yet to be made by industry and the future availability of highly trained scientists with significant track records (and commercial potential).

Some of those interviewed felt that industry will not continue to rely on universities for some of the production-oriented work, and that business is already taking most of the purely developmental research in-house (David Blumenthal and Steven Holtzman, personal communications). These shifts of resources will obviously change the nature of the collaborative efforts. Furthermore, there is some sense that "when the big companies get involved in a big way" (e.g., people; equipment), that "their dependencies on academic scientists will be greatly diminished" (Richard Nelson, personal communication), and that companies are increasingly developing their own capabilities in this area. (Gilbert Omenn, personal communication) However, there is consensus that industry will continue to rely on universities for the cutting edge research and technical breakthroughs.

Some of those interviewed felt that the future growth rate will depend on who is available to collaborate -- or put more cynically: "There is some evidence

of a slow down in the race to fund universities ... most research and most researchers with potential commercial value have already been purchased" (Kenney, 1986, pp. 4-5). Others cited a flattening out of the number of new firms and new scientists in this area as evidence that the trend would not continue at its present rate (Sheldon Krimsky, personal communication).

Summary

All the evidence reviewed in the course of this study suggests that the trend toward research collaborations in biotechnology will continue. However, there is a sense that the pace of that collaboration may decelerate somewhat, and that the nature of the collaborative arrangements may change as a result of:

- Industrial firms conducting more development and product-oriented research in-house in lieu of contracting that portion out to the universities.
- Larger companies growing their own in-house basic research staffs and decreasing their dependence on academic research.

Chapter 2

Types of Collaborative Research Arrangements in Biotechnology

Introduction

University-industry research collaborations in biotechnology and in other fields encompass a wide diversity of types and approaches. Of the entire spectrum of interactions and relationships possible, the particular type that collaborating partners choose depends on the goals and objectives of the respective organizations and their institutional characteristics (Prager and Omenn, 1980). The relevant factors include:

- Industry: the size, structure, and profitability of the industry, the nature of its business, and the progressiveness of its research program.
- Universities: the type, size, and financial health of the university, the relative size and stature of its science and engineering programs, and the orientation of its research and researchers.
- Externalities: geographic location, proximity of the collaborating institutions, regional and state economic development initiatives, the location of university alumni in key industrial positions, and the migration of university faculty to industry and vice versa.

Since 1980, a number of researchers have attempted to develop typologies to categorize the kinds of university-industry interactions that exist. Some of these are generic to all fields (Prager and Omenn, 1980; Peters and Fusfeld, 1981), other categorization schemes are specific to the field of biotechnology (Greenstein, 1983; OTA 1984; Krimsky, 1984; Kenney, 1986). Parenthetically, it is worth noting that with so many radically different models all passing under the same general rubric of "research collaboration", it may never be possible to adequately compass the field in a simple set of categories

(Tornatzky, Solomon and Eveland, 1987). Nonetheless, these typologies are reviewed below.

Generic Typologies

Prager and Omenn (1980) used four categories in their typology of university-industry relationships: Corporate contributions to universities, procurement of services (which included consulting), cooperative research, and research partnerships. Only the latter three categories pertain to research relationships. Peters and Fusfeld (1981) divided university-industry research interactions in all fields into four major categories by primary objective: general research support, cooperative research, knowledge transfer, and technology transfer. A more detailed version of their typology can be found in Appendix D.

Biotechnology Typologies

In its 1984 report on commercial biotechnology, OTA discussed five broad types of university-industry research arrangements in biotechnology. With the exception of the last category, Greenstein (1983) uses a similar typology -- these two categorizations are merged and outlined below:

- Individual consulting arrangements with faculty members -- for salary or equity.
- Industrial associates programs and multi-firm industry-university consortia -- typically several firms provide grants to a single university or university consortium to do research in specified areas over a multi-year period.

- Research contracts -- institution-to-institution cooperative research where a single firm arranges with a university to undertake a specified research activity.

- Research partnerships -- the joint establishment of a research foundation, institute, or long-term collaborative arrangement by an industrial sponsor and a university.

- Private corporations -- innovative approaches to connecting university research to commercial developments (e.g. Engenics; Neogen).

Perhaps the most extensive categorization of existing types of university-industry relations can be found in Kenney (1986). Table 1 below presents his typology.

Table 1. Existing Types of University-Industry Relations

Between individual professors and corporations:
Faculty consulting and research

Between universities and corporations:
Corporate contributions
a. undirected
b. fellowships
c. directed

Industrial procurement of services
a. education and training
*b. contract research
*c. patents

Industrial affiliates such as MIT and Stanford School of Medicine

Cooperative research
a. NSF-funded industry-university research centers such as MIT's Polymer Processing Laboratory

Privately funded research centers
*a. Multicorporate, such as Engenics, Cornell Biotechnology Institute
*b. Single funder, such as MIT's Whitehead Institute

*Long-term contracts such as Monsanto-Harvard, MIT-Exxon, and Hoechst-MGH

*University-controlled companies to exploit research

*Private companies that secure patent rights for resale, such as Research Corporation and UGEN

Source: Kenney (1986), p. 36.
*Important types of arrangements in the biotechnology industry.

Kenney (1986) also provides the most complete list of major biotechnology centers or programs at universities and a summary of the largest university-industry research grants. These are presented in Appendices E and F respectively.

Comparisons Between University-Industry Relationships in Biotechnology and Other Fields

In some ways, the profusion of research collaborations in biotechnology is a natural consequence of the massive infusion of Federal funds after World War II for basic research in fields with medical applications, and the myriad of breakthroughs in science in the 1970s. These factors created "a vast storehouse of knowledge waiting to be used" -- "a phenomenon waiting to happen" (Steven H. Holtzman, personal communication). While this can be said of other fields as well, other sciences -- organic chemistry, electrical engineering, computer science, and physics -- have typically undergone a transformation from a science to the development of new technologies. But none of these earlier fields was developed entirely in academia. As Kenney

(1986) states: "In no other fledgling industry have university scientists played such an all-encompassing role". But there are additional factors that have made industry-university partnerships in biotechnology a somewhat special case.

Krimsky (1984, 1985) maintains that university-industry research relationships in biotechnology are "more varied, more aggressive, more experimental, and more indiscrete" than similar partnerships that have occurred in the fields of chemistry, chemical and nuclear engineering, computer sciences, and microelectronics. There is supporting evidence for this view: with only one exception, all of the major research partnerships between universities and industry have been in biotechnology (Kenney, 1986); and in no other area has so much private capital been raised to establish firms which conduct research, the results of which will be sold as knowledge or products for the private profit of the scientist, or of the university, as owner or co-owner of the firm (Etzkowitz, 1983).

Holtzman asserts that "this new industry of biotechnology requires new organizational structures" and that unlike some other fields where university-industry relationships typically involve multiple companies, collaborations in biotechnology were usually one-on-one relationships due to the product orientation, intense competition, and the potential profits associated with keeping proprietary information secret (personal communication). Krimsky comments that in contrast to a field like microelectronics, where scientists left academia to go to industry, or to

found their own firms, biotechnology was populated by academics remaining within the ivory tower and forming their own start-up ventures.

In addition, the rapidity of breakthroughs in biotechnology has so compressed the time frame between basic research and commercialization that the old continuum no longer exists, and the (always questionable) distinction between basic and applied research has lost its meaning in this field. As Holtzman said, "We are able to do both at once" (personal communication). Furthermore, "much of biotechnology is really a set of research methodologies, so widespread and fundamental in their potential application", that it is thought that "industry will always have to keep in the university just to stay on top of the research and the breakthroughs" (David Blumenthal, personal communication).

According to Nelson, something else quite special is going on in biotechnology. Nelson and his colleagues at Yale recently surveyed businessmen and women in a variety of sectors. They asked their respondents (1) to rate the importance of different fields of science to technical change in their line of business; and (2) to rate the importance of university research to their line of business. While there was not a high correlation between these two items in most fields, respondents in industries related to biotechnology rated both items as important in biology and applied biology. (Richard Nelson, personal communication). This suggests that the links between technical change and university research may be felt most strongly in those fields related to biotechnology.

And, of course, there is the issue of money. Because the science is developing so rapidly and the commercial prospects seem good, the probability of commercial products with great potential of producing large profits in the relatively near term is much higher than it has been in some other fields (Greenstein, 1983). Not surprisingly, therefore, there is a great deal of industrial interest in what's going on in university laboratories these days, and the sheer scale of industry-university cooperation in biotechnology goes well beyond what has typically occurred in other fields. As Greenstein says, "When that kind of money is involved, people pay attention" (Greenstein, 1983, p. 2). This tremendous influx of venture capital in biotechnology has sparked a lot of the collaborative agreements between universities and industry -- agreements that are more likely to involve equity and multiple faculty roles than are similar arrangements in other fields (David Blumenthal, personal communication).

Summary

There seem to be three predominant types of university-industry research relationships in biotechnology:

- Consulting arrangements between individual faculty and firms -- for fee or equity positions.
- Large, long-term grants and contracts between companies and universities in exchange for patent rights and exclusive rights to discoveries.
- The founding of biotechnology start-up firms, often with venture capital, by university professors.

In comparison to university-industry research relationships in other fields, collaborative arrangements in biotechnology are characterized as:

- More varied, more aggressive, more experimental, and, in general, more "extreme".
- Involving new organizational arrangements, such as long-term research contracts and venture capital funded university spinoffs.
- More likely to involve equity and multiple faculty roles.
- More likely to be one-on-one collaborations (e.g., one firm and one university) in lieu of multiple company research arrangements.

Chapter 3

The Potential Benefits of University-Industry Research Collaborations in Biotechnology

> "The interaction of industry with the universities is essential to provide an effective exploitation of the research base. This partnership is critical to our national well-being in an increasingly competitive world marketplace." (White House Science Council, 1986, p. 31)
>
> "In the broadest terms, university relationships with industry are intended to serve the public interest by facilitating technology transfer, improving productivity, and enhancing the competitiveness of the nation in world markets. While there is respect for knowledge itself, the predominant theme of public investment in basic research in this country has been the potential application of such knowledge in industry, agriculture, and medicine." (Omenn, 1983, p. 21)
>
> "In the long run, the establishment of ties between institutions and industrial corporations, large and small, may turn out to be one of the most important scientific developments of the 1980s." (Culliton, 1981, p. 1196)

Introduction

The potential that new economic and social benefits could flow from scientific research has been, over the centuries, one of the key arguments that scientists have used to secure funding and, at times, social stature for the work they do (Etzkowitz, 1983). More recently, scientific research -- especially collaborative research between industry and universities -- has been targeted as one of the critical elements in stimulating technological innovation, enhancing industrial competitiveness, and in achieving sustained economic growth and development, both regionally and nationally. In fact, nearly every statement on America's current economic predicament cites the university as <u>the</u> source of new scientific and technological breakthroughs, and university-industry partnerships as the vehicle through which sustained

economic recovery will be achieved (Kenney, 1986). This is, of course, a rather disproportionate burden to place on only one component of what is usually recognized as a far more complex problem.

Whether or not university-industry collaborative partnerships can in fact "make good" on these claims has yet to be determined. There have been no rigorous, empirically-based, national studies of the outcomes of these collaborative arrangements to date. In part this is due to the only recent creation of many of these collaborative arrangements, rendering such an assessment of outcomes as premature; in part it is because of the threatening nature of such research -- in the absence of data, both sides can claim victory. OTA recently sponsored one of the few studies of the outcomes of collaborative research arrangements in advanced materials, information technology, and biotechnology (Tornatzky, Solomon, and Eveland, 1987). The findings of that study suggest that commercial outcomes -- products and processes -- have been fairly limited to date, and that outcomes are heavily contingent upon how the collaboration is structured and managed.

Yet, regardless of the ultimate economic and social benefits which may flow from university-industry collaborative relationships in this area, there are many nearer-term, tangible benefits that have been cited as accruing to the partners themselves and the public at large from such relationships. Many researchers and commentators have compiled their own lists of the benefits of university-industry research relationships -- some generic to all fields, others specifically oriented to collaborations in biotechnology. These are reviewed below.

Benefits Generic to All Fields

In their survey of U.S. university-industry connections in a variety of fields, Peters and Fusfeld (1981) asked respondents to rank order a list of factors thought to be "motivators" for participating in collaborative research interactions. For industry the top motivators included:

- Access to high quality manpower (e.g., students and professors).
- A window on science and technology.
- General support of technical excellence.
- Access to university facilities.

For the universities, the top motivators included:

- New sources of money that help to diversify the university's funding base.
- Exposure of students to real world problems.
- Better training for the increasing numbers of graduates going into industry.
- Fewer bureaucratic requirements associated with industrial support.

For the university and for its faculty members, Omenn (1983) summarized the potential advantages of these arrangements as: increased income, resources for program expansion, broadened opportunities for students, access to special equipment or research tools, longer-term support for high risk projects, and presumably fewer strings attached than from government funding.

Benefits from University-Industry Collaboration in Biotechnology

In their survey of industrial firms with university-industry research relationships in biotechnology, Blumenthal, Gluck, Louis, and Wise (1986) asked respondents for their list of perceived benefits. Factors perceived by 50% or more of these industrial respondents as benefits "to a great or some extent" (in order of priority) are identified as:

- Help the company to keep current with important research.
- Reduce the costs of mounting R&D programs in a new field.
- Result in product or process licenses.
- Enhance the firm's public image.
- Provide training and staff development for company scientists.

Greenstein (1983) cited several key reasons for industry and university collaboration in biotechnology. From the industry perspective they were:

- Commercialization requires fundamental knowledge of the structure, organization, and mechanisms of expression of the gene system -- knowledge that stems substantially from campus-based research.
- Difficulties in establishing in-house research capability.
- Provides a vehicle for staff training and staff recruitment.

From the university perspective the reasons cited were:

- Improving the level of research and training in applied science.
- Showing an interest in the transfer of technology to industry and greater relevance to society.
- Helping to offset uncertainties of federal R&D support.

Except for expectations of the profound commercial potential for biotechnology-related products in a variety of sectors (e.g., agriculture, chemicals, pharmaceuticals), many of the benefits cited are similar to ones described as motivators in other fields of science.

Interview Data

OTA attempted to refine some of the benefits cited in the literature by asking respondents to give their views on what they perceived to be the benefits for universities, for industry, for individual scientists/professors, for students, and for U.S. industrial competitiveness. Findings from those interviews are discussed below.

Benefits for the Universities

With very few exceptions, money (in a variety of guises) was the first benefit mentioned by all those interviewed:

- "Money for research, the opportunity for equity participation, limited investment in physical plant and facilities, and the associated added income for faculty so that universities don't have to raise their salaries" (David Blumenthal, personal communication).
- "A plurality of sources for funding and equipment" (Gilbert Omenn, personal communication) [the need for plurality was] "fueled by inflation in the late 70s, and a fear -- after the coming to power of the Reagan administration that basic research would be cut" (Martin Kenney, personal communication).
- "Universities are getting money out of it -- industrial funding is a non-trivial proportion of the funding in this area" (Richard Nelson, personal communication).

However, Omenn stressed that the real benefit from university-industry research collaborations is "the capacity to do things neither partner could do before. It's not the money -- this is a very important point." Others, mentioned specific capacity-building benefits that accrue to the universities from such collaborations. These included:

- The added capability for a university to retain faculty members who might otherwise leave, and to attract new faculty and students (David Blumenthal, personal communication).
- The opportunity for smaller, less prestigious universities "outside the club" to build their research base (Steven Holtzman, personal communication).

Since many of the small, less well-known universities often have trouble gaining access to research funds at NIH and elsewhere, the use of industrial capital to build their research capability would obviously be of great benefit. Further studies are needed to investigate the degree to which this is actually occurring on campuses throughout the country.

Finally, several respondents discussed the added excitement and prestige for universities that comes from working on truly cutting edge scientific research and entering into long-term agreements with industry (David Blumenthal, Gilbert Omenn, personal communications).

Benefits for Industry

A 1984 study of biotechnology companies revealed that the investments these companies were making in university research seemed to be yielding substantial benefits to the firms involved (Blumenthal, Gluck, Louis, and Wise, 1986).

According to their survey data, per dollar invested, university research generated more patent applications than investments in company research. Whether these patent applications will result in commercializable products or processes and profits for the sponsoring firms has yet to be realized.

Clearly the commercial potential in biotechnology-related processes and products is one of the primary benefits that industry perceives it will gain through university-industry research collaborations, but it is not the only one that industry values. Those mentioned included:

- Industry has to master this technology to do their own research -- research collaborations with universities allows industry to buy in at a relatively low-cost, without having to recreate the resources and talent already available in academia (Richard Nelson, Steven Holtzman, David Blumenthal, personal communications).
- Academic-business research relationships "make industry more competitive" through "access to brainpower" that they wouldn't normally have (Martin Kenney, personal communication), and "quick access is important due to competition" (Sheldon Krimsky, personal communication).
- These research relationships "help industry obtain capital -- many times industry is selling a dream, this allows them to sell expertise" (Sheldon Krimsky, personal communication).

Thus, in an analogous way to the universities, industry also enhances its own "capacity to do things it could not do before" through collaborative arrangements.

Benefits for Individual Scientists/Professors

As was found in assessing industry benefits, Blumenthal and his colleagues have the only hard data available on benefits received by the individual

scientists who participate in university-industry research relationships. Blumenthal, Gluck, Louis, Stoto, and Wise (1986) conducted a survey of over 1200 faculty members at 40 major U.S. universities. Their findings revealed that biotechnology researchers with industrial support publish at higher rates, patent more frequently, participate in more administrative and professional activities, and earn more than colleagues without such support.

To further capture the positive effects of university-industry research relationships, Blumenthal, et al. asked biotechnology faculty, with and without industrial support, about their own perceptions of the benefits. As Table 2 shows, a majority agreed that such arrangements involved less red tape than federal funding and increased the rate of practical applications from basic research. Their data also suggest some interesting differences between biotechnology faculty with industrial support and those not receiving funding from this source.

Table 2. Benefits reported by biotechnology faculty.

Question	"To some extent or to great extent" (%)	
	Industry support	No industry support
To what extent does industry research support		
Involve less red tape then federal funding	76	51*
Increase the rate of applications from basic research	67	52*
Provide resources not obtainable elsewhere	63	36*
Enhance career opportunities for students	60	43*
Enhance scholarly productivity	41	20*

Produce patents that increase university revenues	41	33

*Significantly different from faculty with industry support ($P < 0.01$). Source: Blumenthal, D., Gluck, M., Louis, K.S., Stoto, M.A., Wise, D. (1986, p. 1364).

A number of researchers have criticized this study because the data are based on survey research which asked faculty to "self-report" behavior that might be embarrassing or mar their reputations as researchers. Although Blumenthal readily agreed that all survey data can be suspect because of the "self-report problem", he pointed out that "unlike a lot of survey research, at least we had a comparison group without industrial connections" and that "there is simply no better way to get the data". (Obviously, the observational method is not an option here.) Further, he said that "the real problem is that it is correlational data -- "we can't say anything about causality". Thus, the question of whether industrial research connections cause enhanced productivity on a wide range of dimensions or, alternatively, whether industry is simply seeking out and funding the most talented faculty, is as yet unanswerable.

Those interviewed clearly felt that money, or rather the things that this increased financial support from industrial sources could buy -- expanded and updated laboratory facilities and the support of an increased number of graduate and post-doctoral students -- was an important benefit that faculty gained through university-industry collaboration. But they also felt that other, less direct, benefits were also significant. Aside from "intellectual stimulation", "the opportunity to stay on the cutting edge of research", and

the ability to receive funds from "a source that required less red tape", respondents discussed:

- The ability to be involved in the commercialization of research -- the sense that a scientist can translate something they have been doing in the lab into something useful (Sheldon Krimsky, personal commuication).
- An increasing awareness that faculty responsibilities go beyond just producing basic knowledge and include seeing that the knowledge is applied and that the research process is expedited (David Blumenthal, personal communication).

Thus, while some faculty members may indeed "be getting rich" because of their industrial connections, there are other, perhaps more subtle and powerful benefits individual scientists/professors are gaining as well.

Benefits for Students

Although the literature on the effects of university-industry collaborations in biotechnology is replete with anecdotes about the problems such relationships can cause for graduate and post-doctoral training, a new study by Gluck, Blumenthal, and Stoto (1986) found that students do not feel that their training is being short-changed or that the quality of their educational experience is being compromised. In fact, the students surveyed generally felt that "the benefits outweighed the risks". In addition, students funded by private firms are more likely than those without industry connections to report patents resulting from their research.

Respondents were asked to comment on the benefits side of the equation for students involved in collaborative research arrangements. Benefits most frequently mentioned were:

- Increased fellowship opportunities for those in school (Richard Nelson, personal communication), and more employment opportunities for students when they graduate -- "not everyone taught can go into academic science" (Sheldon Krimsky, personal communication).

- "The ability to do better and more science, knowledge of industrial applications, and the consciousness of how to do hypothesis testing in the real world" (Steven Holtzman, personal communication).

The Gluck et al. (1986) study is the first hard evidence of potential benefits for students who participate in academic- business research partnerships.

Benefits for U.S. Industrial Competitiveness

Much of the rhetoric about how university-industry research arrangements will be a primary cure for America's sluggish economy and a key factor in regaining technological competitiveness has yet to be proven. To some extent, it is simply too early to tell -- especially in fields such as biotechnology that are still in their relative infancy. However, respondents pointed out several potential benefits for competitiveness that might enure from these kinds of arrangements. These include:

- The massive influx of money in biotechnology has moved this area farther, faster, and has advanced this field of science significantly (Martin Kenney, Richard Nelson, personal communications).

- The movement of basic research closer to commercial development, which is good for the public (Martin Kenney, personal communication).

- The ability for the Federal government to "leverage" the research dollars it commits to basic research, without increasing the aggregate amount of funding (Steven Holtzman, personal communication).

Omenn and Kenney took issue with the way that policymakers view the industrial competitiveness issue. As Omenn said, "It's not us against them, it's us against us". He further stated that most scientists are "internationalists"

that subscribe to "a nicer, pre-desperation attitude", one that presumably enables them to view competitiveness more globally. As he put it: "Managers, not scientists, are worried about industrial competitiveness".

Summary

In summary, the benefits that potentially can accrue to all participants involved in university-industry relationships are obviously many and varied. Omenn (personal communication) summarized this best when he said that there are really four key benefits under which all the others fall:

- The capacity to do things that each partner could not do before.
- The realization of the social compact -- "that the public supports basic research slightly to advance knowledge, but mostly to get some payoff".
- A plurality of funding sources.
- The sheer excitement of being on the cutting edge of a field that has the potential to revolutionize a wide variety of products and processes.

Chapter 4

The Potential Problems of University-Industry Research Collaborations in Biotechnology

"There is justifiable concern that the time may be passing when an individual can produce significant discoveries without outside support and present them as pure gifts to society" (Carnegie Institute, 1982, p. 672 as quoted in Ruscio, 1984, p. 260).

"To the long familiar military-industrial complex a fraternal twin has been added: an academic-industrial complex through which American and multinational corporations siphon the publicly created resources of our universities and thereby convert publicly financed research into private gain" (Minsky, 1984, p. 43).

"The history of technology provides an abundance of examples illustrating the distortion of objectivity when scientific expertise is beholden to the industrial sector" (Krimsky, 1985, p. 49).

"Perhaps the cruelest irony will be experienced by U.S. industry itself. As the university is bought and parceled out, basic science in the university will increasingly suffer ... and the intellectual commons so important for producing a trained labor force and the birthplace for new ideas will be eroded and polluted" (Kenney, 1986).

Introduction

Concerns about the commercialization of academic biomedical research probably reached a zenith around 1981, about the same time that the Committee on Science and Technology of the U.S. House of Representatives convened its first hearing on the subject (Hearings, June 8-9, 1981). The hearings focused on two major issues: (1) whether university-industry research relationships violated scientific and academic freedom and responsibilities, and (2) whether these relationships best served the interests of the American public. By Congressional standards, these proceedings were relatively combative and a number of heated exchanges took place.

However, by the time the Committee convened its second set of hearings almost exactly one year later, some of the initial controversy had subsided (Hearings, June 16-17, 1982). Then Congressman Gore said in his opening remarks: "We do not view such agreements as bad per se, but rather as a development that needs to be examined in detail." However, this kind of detailed examination of the issues that is needed has not taken place. With the exception of a few isolated studies, which will be reviewed below, there is very little evidence to either substantiate or refute the largely rhetorical claims of those who feel great harm is being done to academic science as a result of the new "university-industrial complex."

In the NYU field study of university-industry research interactions, the scientists and administrators surveyed raised a variety of concerns (Peters and Fusfeld, 1981). As shown in Table 3, most of the issues were not mentioned more than 25 percent of the time by either company or university representatives, although academic respondents clearly raised more concerns about the research interactions than their industrial counterparts. With the exception of [balancing] basic vs. applied research (which concerned both parties) and issues of academic freedom (which 23 percent of the university representatives mentioned, as opposed to 0 percent of the company representatives), it is hard to find evidence in the data presented for the other issues Peters and Fusfeld flag as major concerns: research quality, credibility, continuity, and the commingling of funds.

Table 3

Issues Concerning University/Industry Research Interactions Derived from Interviews with Scientists and Administrators at Institutions Surveyed in NYU Field Study

Issues Identified	Percent of Institutions Surveyed Where Representatives Identified These Issues	
	Universities (n=39)	Companies (n=56)
1. Basic vs. applied research	26%	16%
2. Academic freedom: Conflict of interest and/or commitments	23%	0%
3. Should university take equity in a company?	23%	0%
4. Importance of key individual (project director, dean, department manager or chairman, etc.	23%	14%
5. Industry vs. university pay scales	21%	2%
6. Government role as intermediary	18%	11%
7. Tax policy/incentives	18%	23%
8. Industry grants smaller than government grants	15%	0%
9. Ability of small firms to compete with large firms for access to university resources	15%	4%
10. Multi-disciplinary nature of cooperative efforts	15%	5%
11. Restrictions on public universities	13%	11%
12. Peer review	8%	9%
13. Commingling of industry and government funds in support of university research	5%	0%
14. Credibility of the university	3%	2%
15. Collective industrial support and anti-trust regulations	0%	4%

Source: Peters and Fusfeld (1981), p. 112.

The Potential Problems in Biotechnology

Kenney's 1986 book, Biotechnology: The University-Industrial Complex, contains a lengthy discussion of the potential problems for universities and faculty members engaged in collaborative arrangements. These can be summarized as:

- Impacts on the university's research agenda -- such as the potential for professors to orient their research towards products that could have commercial value or the shifting of research to accommodate corporate sponsors.
- Conflicts of interest -- such as the use of university equipment for private gain or taking undue time away from university responsibilities.
- The exploitation of students as "merely inexpensive labor" or the outright neglect of students by faculty who become increasingly involved in commercial projects.
- Interruptions in the free flow of information and materials among colleagues because of patent-induced publication delays, trade secrets, and other proprietary inhibitions. This is called the "publish or profit" problem.

Yet in the text, Kenney (1986) cites numerous refutations of the problems. For example, in discussing the issue of secrecy and the free flow of information he states: "Secrecy is not new in academia -- the quest for grants, prizes, and status makes secrecy until publication important" (p. 110). However, he does feel that this secrecy in academia has not been as "obsessive" as it has until recently when industrial concerns were involved. As for impacts on the research agenda, Kenney questions what he calls "the myth of the selfless scientist" -- that rare academic who truly seeks knowledge for its intrinsic value alone. In discussing the effects of university-industry relationships on students, Kenney states: "the

exploitation of students for a faculty member's academic advancement is traditional". However, he goes on to say that "the professor's potential to profit financially from a student's work places the relationship in a very different light" (p. 121). Even in the area of conflicts of interest, Kenney states that such conflicts "have always been a feature of the university and merely express the fact that certain branches of research are closely linked to commerce" (p. 114). Most of these arguments and counter-arguments also were expressed by those interviewed.

A review of Omenn's (1983) list of potential risks for the university and its faculty raises two additional concerns not discussed above: creating imbalances of faculty, students, and space, and losing public confidence and jeopardizing government funding. Krimsky (1984) and Ruscio (1984) add a third concern to the list: the loss of the norm of disinterestedness -- "the detachment that scientists supposedly bring to their work" (Ruscio, 1984, p. 268).

Krimsky sees a critical need for a "disinterested intelligentsia" -- scientists free from corporate involvement to whom the public can turn for objective evaluations of technological risks, goals, and directions. His research shows that the number of "dual-affiliated" scientists in biotechnology is in fact sizable. However, Krimsky admits that he has no hard evidence that academics with industrial ties are in fact less objective in their judgments, or less disinterested in scientific truth (Sheldon Krimsky, personal communication). Critics have termed his research "damnation by affiliation".

Once again, the only hard evidence available on the risks of university-industry research relationships in biotechnology comes from Blumenthal and his colleagues. Findings from their faculty survey reveal that faculty with industry funds are much more likely than other biotechnology faculty to report that their research has resulted in trade secrets and that commercial considerations have influenced the choice of research projects by academics (Blumenthal, Gluck, Louis, Stoto, and Wise, 1986). Table 4 below presents the risks reported in their study by biotechnology faculty with and without industrial support.

Table 4. Risks reported by biotechnology faculty.

Question	"To some extent or to great extent" (%)	
	Industry support	No industry support
To what extent does industry research support pose the risk of:		
Shifting too much emphasis to applied research	70	78*
Creating pressures for faculty to spend too much time on commercial activities	68	82**
Undermining intellectual exchange and cooperative activities within departments	44	68**
Creating conflict between faculty who support and oppose such activities	43	61**
Creating unreasonable delays in the publication of new findings	40	53**
Reducing the supply of talented university teachers	40	51*
Altering standards for promotion or tenure	27	41**

*Significantly different from faculty with industry support ($P < 0.05$).
**Significantly different from faculty with industry support ($P < 0.01$).
Source: Blumenthal, D., Gluck, M., Louis, K.S., Stoto, M.A., Wise, D. (1986, p. 1365).

Findings from their industrial survey (Blumenthal, Gluck, Louis, and Wise, 1986) suggest that the companies that sponsor university research also perceive potential risks in university-industry research relationships. Those perceived by over 20% of the firms as a potential risk "to a great or some extent" were:

- Risk a poor payoff in marketable products (62%).
- Risk a loss of proprietary information (58%).
- Take too much effort to monitor and control (42%).
- Run the risk that universities may choose to withdraw from relationship before the firm receives anticipated benefits (21%).

In general the perception of potential problems that can result from university-industry collaborations in biotechnology are not that different from those cited in other fields. However, the degree and frequency with which these problems are occurring is perceived to be intensified in biotechnology.

Interview Data

Interviewees are asked to separate potential problems at the institutional and at the individual level. Respondents described what they thought were the major problems of research collaboration in biotechnology for universities, for industry, for individual scientists/professors, and for students. Findings from those interviews are discussed below.

Problems for Universities

Comments about the problems universities are experiencing in collaborative arrangements ranged from "the problems are many" to "the problems have been beat to death". Respondents emphasized that the key issue for universities is whether and to what degree they should continue to be "an ivory tower" -- detached from the real world of business. Some of those interviewed wondered whether this idealized (or idolized) kind of academic environment ever existed at all. Yet regardless of their points of view on this issue, there was consensus that universities are indeed being changed and transformed by their research relationships with industry. Two contrasting comments illustrate the diversity of views as to whether this transformation is a positive or a negative evolutionary step for the university:

- "Will the goals and values of the university be transformed in such a way that its essential qualities will be lost?" (Martin Kenney, personal communication).
- "What are the essential qualities of a university? Increasing the storehouse of knowledge is one of them. If that knowledge is then used by someone, it's a win-win situation" (Steven Holtzman, personal communication).

Blumenthal raises the issue that this perception of change in the universities could cost some of them their current tax-exempt status. He cited upcoming Congressional hearings on this issue as evidence that some policymakers are beginning to question whether universities with strong commercial ties still deserve such status.

The second most frequently cited problem was secrecy. Krimsky maintains that the difference in academic environments today is that "colleagues can't speak

to each other not because of [the information's] intellectual potential, but because of its commercial value" (Sheldon Krimsky, personal communication). But Holtzman disagreed: "I don't see where a delay in publication of six months makes any difference. Besides, academic competitiveness has always been secretive." He went on to say that trade secrets tend to be on the production side, not the basic research side and that the trade secret problem in the universities will diminish now that many corporations have begun to bring the more development-oriented production activities in-house (Steven Holtzman, personal communication).

A number of respondents including Krimsky, Kenney, and Nelson were concerned about inter-department and intra-department competition for scarce resources and the potential imbalances in resource allocation that university-industry collaborations can cause. Kenney questioned whether the presence of such relationships would cause some fields within the university to "atrophy" because of the relatively paltry share of resources they received from the university.

One potential concern raised by Kenney and discussed in his 1986 book has the potential of doing great harm to the university: What will happen if a large agreement between a university and a company (e.g., Monsanto-Washington University or MGH-Hoescht) expires and the company decides not to renew? Obviously, universities also put resources into such arrangements -- they build facilities, hire staff, and redirect resources. As Kenney said, "If industry pulls out the university is left holding the bag." Furthermore, he went on to say that the mere threat of a pull-out could place universities in

a "negative bargaining position" when it comes time for industry to renew a large agreement (personal communication).

Problems for Industry

The majority of respondents either did not perceive that there were any problems for industry that could come from university-industry research collaborations or chose not to comment on them. Most simply stated that they "hadn't thought about that issue much", or as Nelson said: "my bet is that industry will take care of itself just fine". The only concern voiced for industry was whether these academic-business partnerships in biotechnology will result in the revolutionary new products and processes currently envisioned. Most felt "the jury was still out".

Problems for Individual Scientists/Professors

The most frequently cited problem for faculty involved in collaborative research relationships with industry was the potential conflicts inherent in having "mixed allegiances" which it is feared results in faculty spending a disproportionate amount of time on applied research and commercial interests. In our interview with Kenney, he referred to a statement made by Donald Kennedy, President of Stanford University, before the U.S. House of Representatives Committee on Science and Technology Hearings on this issue in 1981:

> "A large number of our faculty members ... have recently concluded or are now contemplating individual arrangements with mostly young, new biotechnology firms. ... We are going to have to measure over

> the next few years how much of a real loss is experienced in terms of fractional faculty time and energy committed to the research enterprise and to the research training in the university. We are not losing whole people. What we are concerned about is what the ultimate landscape will look like in terms of the loss of parts of people."

This argument is called "the more, the less" hypothesis by commentators -- the more one engages in outside commercial activities, the less one devotes to university responsibilities. However, the conclusions of Blumenthal, Gluck, Louis, Stoto, and Wise (1986) seem to suggest an opposing hypothesis -- "the more, the more". According to their data, biotechnology faculty with industrial support exhibit enhanced productivity on a wide range of dimensions including university activities and do not show any significant differences in teaching time. Of course, "teaching time" may not be the appropriate measure of effects -- perhaps a factor of greater relevance is the content and quality of that teaching, and the material contained in the coursework itself.

In addition to the very real conflicts of interest that can arise when faculty divide their time and potentially their loyalties between academic and commercial pursuits, those interviewed also commented on concerns of a more perceptual nature -- ones they feel are deeply affecting life in university departments where connections to the biotechnology industry are strong. Some respondents discussed the "bad vibes" and "tones of hucksterism" that can pervade such departments. Nearly all those interviewed talked about the "jealousies" between "the academic haves" (those with industrial support and especially those with their own biotechnology ventures) and "the academic have-nots" (professors without business connections). In some university

departments resentment has grown to such a point that entrepreneurial scientists have been forced to resign.

Probing further as to the source of some of these concerns, respondents were asked whether the crux of the issue wasn't really money -- the sense that there is something wrong with being a "rich professor". (Indeed, a number of those interviewed were in fact "queasy" about the personal wealth that some of the entrepreneurial scientists in biotechnology are accumulating). Blumenthal responded that, while jealousy was certainly an important source of the controversy, the jealousy is not based on the personal wealth of the individuals involved, but rather the increased research budgets, glamour, and power within the university (e.g., the ability to win space and facilities) that such individuals' possess.

Krimsky took this concern one step further pointing out that the leading scientists in a field are always seen as "role models". It is his feeling that in biotechnology "the leading scientists (like Gilbert and Baltimore) have taken the initiative in developing the new consciousness in academic circles and they have done it proudly, not furtively". To him this suggests that these leaders are role modeling the behavior that "it is OK to be rich, famous, and an academic".

Problems for Students

There is a great deal of discussion, but very little reported in the literature about what impacts university-industry relationships are having on

students and post-doctoral fellows. Some respondents, such as Omenn, said that potential concern about students is "the one problem area I worry about the most." The fear that students could be exploited by commercial interests or the pecuniary demands of their professors, and that their education and training may be consequently compromised, was often expressed in the interviews. Yet the exploitation of graduate students was also cited as a traditional norm in many academic departments. As one respondent said, the myth that "academic scientists care about students is crazy".

A recent and as yet unpublished study (Gluck, Blumenthal, and Stoto, 1987) tried to add some empirical data to an area in which the only evidence of problems for students to date has been in the form of newspaper articles and anecdotal stories. Gluck et al. conducted a survey of 693 graduate students and post-doctoral fellows at six research-intensive U.S. universities. Their focus was on assessing the effects of industry-sponsored university research in the life sciences, and more specifically in biotechnology, on students. The data suggest the existence of some risks: students with industrial support published about a third fewer papers, reported more significant delays in publication, and discussed inhibitions in discussing their work with colleagues more frequently than their peers.

Summary

Many who take a negative view of university-industry research relationships seem to be arguing for a return to a simpler time -- when academics were academics, and businessmen were businessmen. This nostalgia is reminiscent of

a story Etzkowitz relates in his 1983 article in Minerva. In discussing the fact that "the sale of scientific knowledge by most scientists was eschewed in the nineteenth century", Etzkowitz tells of an encounter between Napoleon III and Pasteur. Napoleon III was said to have asked the esteemed scientist why he did not turn his discoveries to legitimate profit. Pasteur's reply: "In France scientists would consider they lowered themselves by doing so" (Bernal, 1953, p. 86 as quoted in Etzkowitz, 1983).

Times have clearly changed, and both the internal and external demands on the university are increasing and sometimes conflicting. Perhaps the most blatant example of those changes and the conflicts that can ensue is the ever-closing gap between business and academia in American biotechnology. To say that universities are suffering from some very real growing pains is not to dismiss the importance of these changes or the angst of some individuals affected by them. However, "the real question is what is the proper role of the university in the 1980s -- as opposed to the 1500s?" (Steven Holtzman, personal communication).

Furthermore, it must be said that even though industrial support for university research in biotechnology has clearly changed the dynamics of that field at the individual and institutional levels, any funding source has the potential of influencing the research agenda and those that conduct the sponsored research. This is not a new issue either. History, going back to at least the passage of the Morrill Act in 1862, and surely to government-university research partnerships during World War II or the current support of numerous physics professors by the SDI program, clearly shows that

collaborating partners often use the universities for their own purposes, missions, and objectives. In his testimony before the House Committee on Science and Technology hearings on this topic in 1981, Dr. Lamont-Havers, Director of Research, Massachusetts General Hospital, addressed this issue:

> "In many respects, I believe that the arguments which are going on now within academia, the soul searching, the concern of the impact [of] industry on academia, how this is going to destroy values is very reminiscent of the same type of arguments which went on 20 or 25 years ago when large amounts of Federal funds began to flow into the academic institutions" (Hearings, 1981, p. 90).

In this regard, money from industry is probably no different than support from other sources -- each has the potential power to influence and corrupt. As Omenn wrote:

> "To be realistic and not too romantic about the often-troubled past, we should note that universities have found themselves negotiating over or adjusting to requests and requirements of the funding source, whether wealthy individuals, foundations, industry, or government" (Omenn, 1983, p. 21).

One respondent summarized by saying: "If someone wants to sell their soul, they will. If someone wants to be bought, they will be bought. But just because there is twilight doesn't mean I can't tell night from day" (Anonymity requested, personal communication).

Finally, problems such as academic secrecy and competitiveness, the exploitation of students, and incursions into the purity of science and scientists are not new to the university. However, many feel that the magnitude and pervasiveness of the problems as exhibited in biotechnology has changed for the worse. Nelson, for example, states that we should really be asking not <u>what</u> are the problems, but rather: "Changed, compared to what; and

what is the degree of those changes"? It would appear that university-industry research relationships in biotechnology are so controversial because:

- The sudden awareness of the technology's potential.
- The sheer lucrativeness of the contracts,
- In many cases they seem to have sparked an extreme case of many of the ills that have plagued the ivory tower for decades.

Chapter 5

Variations in the Benefits and Problems of University-Industry Research Collaborations in Biotechnology

Introduction

Many of the researchers and commentators who discuss the benefits and the problems of university-industry research collaborations in biotechnology often speak as if academia and business were monolithic entities. Obviously, this is not the case. Universities vary enormously in their structures, values, objectives, and their orientations and responses toward collaborative research. And the diversity of U.S. industrial firms on these dimensions is probably even greater. Consequently, the type of university-industry research arrangement that "works" for an Eastern Ivy League university may be very different from one that would fit in at a land grant college in the south or the midwest; and the motivations and expected outcomes of a large multinational corporation that collaborates with a university -- such as Monsanto's agreement with Washington University -- undoubtedly would vary greatly from those of a start-up venture like Embryogen and its relationships with Ohio University.

Because these differences may affect the kinds of benefits and problems experienced by collaborating partners in research arrangements, it is important to go beyond the generalities, and to try and document some of these "variations". The findings presented below are taken from both the literature and the interviews.

Variations Among Types of Collaborative Arrangements

The specific concerns associated with university-industry research relationships in biotechnology depend largely on the type of alliance under consideration. (Olson, 1986) As was discussed earlier, the arrangements vary considerably in the activities involved. The Roundtable (1986) report characterized the range of activities as:

- Some are largely concerned with basic research.
- In other arrangements, the work is largely applied, intended to solve or illuminate a well-defined problem.
- Some involve very little research on the part of academics, but rather, are focused on providing consultation or other kinds of assistance to a company.
- In some cases, constraints are imposed to limit faculty entrepreneurship, while in others, the arrangement is designed to channel and facilitate that entrepreneurship.

Research relationships vary in organizational structure as well -- one-on-one consulting, industrial associates programs, research consortia, long-term research partnerships, and new ventures formed by academics differ significantly in terms of their goals, management and governance, and presumably the benefits and problems experienced by their participants. In addition, the same professor may be involved in a variety of such arrangements simultaneously, sometimes with the same company, such as the case of a professor with significant equity interest in a company who serves as a consultant to the company, and has at the same time been awarded a research grant from the firm as well. Kenney (1986) discusses this situation as the "worst case scenario".

In a recent OTA study, (Tornatzky, Solomon, and Eveland, 1987) the particular type of organizational structure was not highly correlated with benefits or outcome measures. It would seem that the same could be said for the problems side of the equation. What is more likely (although additional research is clearly needed in this area to say with certainty) is that the potential problems for the university and its faculty may be tied to two things: the degree to which a particular arrangement of any type interferes with the duties and responsibilities of a faculty member to his or her university, and whether the agreement is made at the individual or institutional level. However, it must be said that from an industrial point of view, benefits are in part tied to these two factors as well -- only the direction of the correlation is probably reversed.

Although all respondents agreed that the benefits and problems vary according to the type of relationship, there was no consensus on which type is the most problemmatical for its participants. For example, while Nelson was enthusiastic about the Centers' approach (e.g., the NSF model) to university-industry collaboration, in which university, industry, and Federal funds are commingled, Kenney viewed such consortia with caution: "they become almost separate parts of the campus -- a self-enclosed community" which from his perspective inhibited communication and interactions among departments. Whereas some of those interviewed perceived long-term research partnerships to be less problemmatic and more desirable, others were concerned with the major changes in structure and the imbalances in resource allocation that such agreements can cause.

And unlike a number of respondents who felt that consulting arrangements between faculty and companies was a norm that universities had adjusted to (as long as the so called "one-fifth rule" is not abused), Holtzman labeled consulting as university "rape" -- "though it looks clean on paper, there is no return to the university, since there is no overhead on a consulting contract." He went on to say that universities can benefit more [at least monetarily] from forming a start-up company -- the revenues from which can be held in the institution's endowment. But Holtzman was clearly in the minority in viewing start-ups as potentially benefiting the university. The majority of those interviewed expressed grave doubts and deep fears about the impacts of entrepreneurial scientists and their venture activities on the ivory tower.

Variations Among Industrial Partners

It is obviously not possible to explore all the differences among industrial partners that can affect university-industry research collaborations in biotechnology. Furthermore, there are times when the same company enters into different types of agreements with separate universities, each characterized by its own pattern of interactions and outcomes. An example of this is Monsanto's agreements with Harvard and Washington University. Therefore, we decided to concentrate on what seems to be one of the most important factors -- the size of the collaborating partner.

Blumenthal, Gluck, Louis, and Wise (1986) compared university-industry research relationships in biotechnology that involved small firms to those in

which large firms were the collaborative partner. In general, their findings suggest that collaborations with small firms seem to constitute the greatest gamble for universities. Compared to larger firms in their study, small firms are more likely to:

- Support faculty with significant equity in their companies;
- Report the occurrence of trade secrets; and
- Fund projects of very short duration.

On the other hand, Blumenthal et al. discuss the fact that the financial benefits of these relationships could be quite large down the road, "since these arrangements seem to produce many more patent applications per dollar invested than do relationships with large firms". Of course, as they point out, "it is far from certain that the applications for patents held by universities will ever produce profitable licenses". Blumenthal further stated that "research relationships with large companies were smoother, less complicated, contained less conflicts of interest, but probably produced less payoff" (David Blumenthal, personal communication).

In commenting on the issue of the size of the industrial partner, Krimsky said: "the benefits are much higher to individual scientists with large companies -- there is a steady stream of money over a long-term horizon." However, not all our respondents perceived small firm collaborations as potentially risky. Nelson discussed the fact that the orientation toward collaborating with small firms depends on the type of university involved and the way that institution perceives its missions vis a vis industry. As he put it: "I am scared about collaborating with small companies if I look at it

from the point of view of a university administrator at Yale or Columbia, but if I am at Georgia Tech, I like it just fine." Holtzman saw more potential risks in the kinds of agreements that large companies enter into with universities: "a large company can buy a department, but a small company can't."

Variations Among Sectors or Areas of Research

The study also explored the degree to which university-industry research relationships in biotechnology vary by sector or area of research (e.g., agriculture; chemicals; pharmaceuticals). However, little is known to date about sector or area variations in biotechnology. The most frequent response to this question was: "I don't know -- but it is a very interesting question." Hence, the following is speculation, not fact.

Kenney conjectured that the major sector difference is in orientation and focus: product vs. process. Since companies are most interested in products, which can yield the greatest potential gain, the most frequent and intense university-industry research collaborations seem to be taking place in pharmaceuticals. In agriculture, while there are proprietary plants, the research problems are thought to be more complex, the products envisioned more long-term, and the degree of collaboration is not as intense. Kenney went on to say that in chemicals, where the research is more applied, a large proportion of the research can be done in corporate labs or through consulting -- decreasing this sector's dependency on university-industry research relationships.

Markle and Robin (1985) argue that biotechnology firms have already altered the nature of problem selection by academic scientists -- problems dependent on the elaboration of technique, not theory, are emphasized. Consequently, in university-industry research relationships, corporations are focusing on the development of biologicals (e.g., enzymes; pharmaceuticals) because of the likelihood of more rapid commercial payoff. Their analysis suggests that problems requiring that substantial theoretical obstacles be crossed before technical breakthroughs can be achieved (e.g., the control and transfer of nitrogen fixation in the agricultural sector) are receiving less immediate attention in collaborative research partnerships.

Variations Among Universities in their Responses to Collaborative Research Arrangements

Just as these collaborative arrangements vary tremendously depending on their form, structure, and area of research, so too do universities exhibit a great deal of diversity in their responses to the benefits and problems which can result from university-industry research relationships. Universities vary greatly on a number of significant dimensions which affect their involvement with industry in research arrangements. These include:

- The amount of time allowed to faculty for outside consulting, or for the management and/or involvement in entrepreneurial activities.
- The degree to which faculty can use university equipment, facilities, and staff (including students) in non-academic, commercial research.
- Sanctions against, or incentives for, universities to become financially involved in the start-up or spinoff ventures of faculty (e.g., equity interests in ventures seeded; funding incubator centers; etc.).

- Whether the university, industrial sponsor, or individual scientists retain intellectual property rights and/or the exclusivity of such patents, licenses, and trade secrets.
- The amount of time deemed acceptable to delay publications prior to or simultaneous with patent filings.
- Whether university scientists or industrial sponsors (or some combination of the two) set research priorities and the research agenda.

When asked what lessons had been learned from collaborative research arrangements in biotechnology, half of those interviewed suggested that the lessons are "that some things have gone too far". Krimsky commented that even though "some universities have set different boundaries than others -- some things are clearly 'out of bounds'" (Sheldon Krimsky, personal communication). Nelson reiterated this point when he said, "We need a pluralistic university system, but even [name of university withheld] will have to have some standards or they will find themselves treated as the concubines of industry." He went on to say that the largest, most prestigious universities must be the ones to stand up to the potential risks of industry-university collaboration and set the standards for other institutions to follow (Richard Nelson, personal communication).

Yet, regardless of these calls for self-regulation, there are few hard and fast norms in place throughout the academic community on the six dimensions just described. Rather, each institution is meeting the challenge of setting its own boundaries of acceptability in ways that are consistent with its characteristic culture and mission. Some of the suggestions that have been made for where boundaries should be set are contained in **Chapter 8: Recommendations and Policy Issues.**

Summary

The assumption that a continuum can be constructed to characterize the nature of collaborative research arrangements in biotechnology, and that problems would intensify as the ties between academia and business intensified, is naive. It is not that simple. There are clearly problems and benefits at all ends of the continuum. Furthermore, rather than a linear continuum, there exist multiple axes at any moment in time (e.g., type of arrangement; size of industrial partner; university culture; area of research). This may not be a parsimonious or tidy way to characterize the issues, but it is realistic.

Chapter 6

Foreign Company Research Collaborations with the U.S. in Biotechnology

Foreign Company-U.S. University Research Connections

Although a few collaborative research relationships between foreign companies and U.S. universities have been quite public and covered in-depth in the open literature -- such as the agreement between Hoechst and Massachusetts General Hospital or the one between the Medical University of South Carolina and Chugai -- most are neither well known nor well documented. Although a database search (Appendix G) uncovered information concerning academic-industrial research relationships on an intra-country basis (e.g., Japanese firms entering into agreements with Japanese universities), no publications documented U.S. university-foreign company agreements.

The question of what information exists on foreign company-U.S. university research connections was posed to those interviewed. None of the respondents knew of any existing sources on the topic, although one commented that original data could be collected from company prospectuses, university documents, and through extensive interviews with industry representatives and university administrators. However, he cautioned this would be an extremely expensive exercise. Although no single, accessible source could be found that documents foreign company research collaborations with U.S. universities, a number of analyses of the trends in foreign company research agreements with U.S. firms are available.

Foreign Company-U.S. Industry Research Connections

To understand the trends and forces behind U.S.-foreign research relationships, one needs to examine the differences between the U.S. biotechnology enterprise and its foreign counterparts. The United States has the largest biotechnology effort. Most of the firms, universities, and other institutions that work in biotechnology are based in the U.S. and the U.S. government is the world's largest financial supporter of this research. But the most distinctive characteristic of biotechnology in the U.S., as compared to Europe or Japan, is the large number of "start-up" firms dedicated specifically to researching and commercializing biotechnology. The vast majority of the world's start-up firms are located in North America; most in the U.S., and secondarily in Canada (Genetic Engineering News, 1986). Japan and Europe have relatively few such firms.

The presence on this continent of so many entrepreneurial firms is generally attributed to the availability of large sums of venture capital. Conversely, in Europe, biotechnology projects are funded by more traditional corporate sources and often with the extensive support and coordination of government (Dibner, 1986). Japan's biotechnology development relies even more heavily upon government supervision, through its Ministries of Trade and Industry (MITI), Agriculture, Forests, and Fisheries (MAFF), and the Science and Technology Agency (STA) (Dibner, 1985; OTA, 1984). Thus, in contrast to the U.S. biotechnology industry, which is characterized by a large number of entrepreneurial ventures, intense competition, and tremendous redundancy, the efforts of other countries (especially Japan) are more highly structured and

consequently less duplicative. As Kenney (1986) wrote: "the ultimate contest in biotechnology will be between the U.S. and Japan to see which system can diffuse innovation more quickly".

Presently in Europe, over 250 firms perform research, development, and production activities in biotechnology, with the greatest concentration of efforts in the United Kingdom, West Germany, and France (Dibner, 1986; OTA, 1984). Italy and the Netherlands both have strong government-cultivated initiatives in biotechnology, while Switzerland has strong corporate initiatives because it is home to 3 of the world's 15 largest pharmaceutical companies (Dibner, 1985; OTA, 1984; Dibner, 1986; Genetic Engineering News, 1986).

The Japanese government focuses upon specific national targets for biotechnology development, and coordinates various sectors of the nation to interact more efficiently. It tries to erode structural barriers between research, development, and commercialization of biotechnology by, for example, sponsoring joint ventures between industry and academia, or research on scale-up techniques to bridge laboratory results with industrial production. Presently, Japan leads the world in fermentation technology which alone provides a large skilled workforce in biotechnology. The Japanese Biotechnology Development Center estimates $60.7 billion in Japanese biotechnology-related sales by the year 2000 (Dibner, 1985).

Clearly, Japanese firms and their government agencies heavily emphasize R&D. For example, Japanese pharmaceutical companies spend about 50% more of their

sales on R&D than U.S. pharmaceutical firms (Dibner, 1985). However, in most fields, Japan still lags behind the U.S. in performing basic and pioneering research, and biotechnology is no exception. To compensate for this lag, it is argued, Japan participates in and sponsors collaborative research in the United States.

Dibner has constructed the most complete database on joint agreements between U.S. and foreign biotechnology companies. Table 5 below presents his data on contractual agreements between U.S. biotechnology firms and major Japanese companies that were announced between 1981 and 1984. Table 6 below presents joint agreements between U.S. biotechnology companies and European companies involving pharmaceutical products that were signed between 1982 and 1985.

Table 5. Contractual agreements between U.S. biotechnology firms and major Japanese companies.

Biotechnology firm	Japanese company	Products involved
Biogen	Shionogi	Interferon, IL-2, HSA
	Fujisawa	Tissue plasminogen activator
	Green Cross	Hepatitis B vaccine
	Suntory	Tumor necrosis factor
	Teijin	Factor VIII
Centocor	Toray	Hepatitis diagnostics
Collaborative Research	Green Cross	Urokinase, interferon
Genentech	Mitsubishi	Tissue plasminogen activator
	Toray	Interferons
Genetic Systems	Daiichi	Diagnostics for blood disorders
Genetics Institute	Chugi	Human erythropoietin

Genex	Yamanouchi	Fibrinolytic agent
	Green Cross	HSA
	Yoshitomi	IL-2
	Mitsui Toatsu	Urokinase
	Mitsubishi Chem.	HSA
Hybritech	Teijin	mAb's for cancer treatment
	Green Cross	Immunoglobulins
	Toyo Soda	mAb diagnostics

Source: Mark D. Dibner, "Biotechnology in Pharmaceuticals: The Japanese Challenge," Science, Vol. 229, September 20, 1985, p. 1233.

Table 6. Joint agreements between U.S. biotechnology companies and European companies.

U.S. Company	European Company	Product
Biogen	Bioferon (West Germany)	IFN
Biogen	Burroughs-Wellcome (United Kingdom)	Vaccine
Biogen	KabiVitrum (Sweden)	Factor VIII
Centocor	Hoffmann-LaRoche (Switzerland)	mAb's
Cetus	Roussel Uclaf (France)	Vitamin B_{12}
Collaborative Research	Sandoz (Switzerland)	KPA
Damon Biotech	Hoffmann-LaRoche	mAb's
Flow Labs	Bioferon	IFN
Genentech	Gruenenthal GMBH (West Germany)	Urokinase
Genentech	Hoffmann-LaRoche	IL-2
Genentech	KabiVitrum	hGH
Genetics Institute	Speywood Labs (United Kingdom)	Factor VIII
Genetic Systems	Sandoz	IL-2
Genetic Systems	Cutter Labs (Bayer)	MAb diagnostics
Genetic Systems	Institut Pasteur (France)	Diagnostics
Genetic Systems	Miles Labs (Bayer)	mAb's
Genex	KabiVitrum	HSA
Genex	Schering AG (West Germany)	Blood protein
Hana Biologics	Recordati S.p.A. (Italy)	mAb diagnostics
Hybritech	Boehringer-Mannheim	mAb's
Immunex	Behringwerke (Hoechst)	CSF
Unigene Labs	Sigma-Tau S.p.A. (Italy)	Diagnostics

Source: Mark D. Dibner, "Biotechnology in Europe," Science, Vol. 232, June 13, 1986, p. 1371.

The tables above list only a fraction of the cooperative research agreements between foreign companies and U.S. biotechnology firms since many are still unknown, Dibner primarily concentrated on pharmaceuticals, and new research relationships are reported in the literature every month. A recent article quotes the chief executive of Celltech, a British firm that just formed a U.S. subsidiary, Boots-Celltech, Inc.:

> "The U.S. is usually where things start and then the world learns from it. The trends in world heathcare start in the U.S., and if you're not linked into it, you're in danger of not being on target" (Klausner and Dixon, 1986).

While this executive was speaking of the American market and its demand, no doubt it is partially true of research as well. Many non-U.S. firms establish research partnerships with U.S. laboratories in part because of their track record of discovery. One study found that half of the technical exchanges between Japanese and American firms which it reviewed were research contracts. Inevitably in these cases, the research is performed in the U.S. and financed by the Japanese (Peters, 1986).

Foreign-U.S. Research Collaborations and Industrial Competitiveness

Some argue that such research relationships lead to a loss of U.S. competitiveness, since they fear that Japan is better positioned to apply and commercialize the results of research conducted in U.S. universities and biotechnology firms. Further, while the method and extent of financing research depends upon each specific research agreement, it is argued that much of the U.S.'s research capacity is the result of significant public investment in the training of scientists and the equipping of laboratories. The failure

of the U.S. to capitalize on its investment by not being the first to develop commercial products, or the loss of these opportunities to other nations is argued by some to cost this country significantly more than it gains (Dibner, 1986; Dibner, 1985; Novis, 1983). However, several respondents had a different view of the role of international research relationships in global competition. In essence, Omenn and Kenney both argued that collaborative research partnerships did not result in the hemorrhage of scientific information and technology that is traditionally claimed, rather they felt that such partnerships advance and expedite the research process for all participants and can result in a win-win situation even for competing nations (Gilbert Omenn and Martin Kenney, personal communications).

As was evident during Congressional testimony, the research agreement between Hoechst, the world's largest pharmaceutical company, and the Massachusetts General Hospital at Harvard evoked concerns about competitor nations gaining strength through collaborative research partnerships. The House Science and Technology Committee's Subcommittee on Investigation and Oversight inquired if Hoechst was not "skimming off the cream" of substantial U.S. public investment in research at that hospital. Hospital officials argued that Hoechst would gain exclusive license only to patents derived directly from the research Hoechst had funded. As to whether such relationships secure "free enterprise" or only "free-riders" is an unsettled economic debate. If in fact such an agreement is unfairly advantageous to Germany, not every German knows it. The Hoechst-MGH agreement was "widely criticized by many German scientists who feel the money should -- and could -- have been spent domestically" (Dickson, 1982).

A related issue is the potential problems for U.S. industry caused by the participation of foreign companies in research consortia and centers. Although this was one of the issues discussed in the 1986 report of the University-Industry Research Roundtable, that report did not reach any conclusions on whether foreign participation in such collaborative programs was a problem or a benefit. Instead the report stated that "each case should be judged on its own merits". A previous OTA working paper suggested that university and industry partners in collaborative research arrangements tend to welcome the participation of most foreign firms with the exception of the Japanese (Tornatzky, Solomon, and Eveland, 1987). Since multiple research consortia are not the norm in biotechnology, the participation of foreign firms may be less of a problem in that field than in others (e.g., microelectronics).

Since it is argued by some that the presence of foreign partners in U.S.-based research is disadvantageous for the U.S., one might think that the U.S. presence in research abroad, conversely, would be advantageous to the U.S. But this is not necessarily so. First of all, U.S. firms do not conduct as much research in Europe or Japan, and there are no clear examples of U.S. firms that have the majority of their biotechnology research facilities in Europe (Dibner, 1986). Secondly, it is said that U.S. firms in Europe are themselves transferring technology out of the U.S. since U.S. firms are generally not allowed to export drugs which have not received U.S. Food and Drug Administration (FDA) approval (Dibner, 1986). The 99th Congress passed the Drug Export Amendments to address this issue.

Summary

There are no comprehensive databases that detail foreign company research agreements in biotechnology with U.S. universities and industrial firms. The information that is available suggests that foreign firms enter into international research agreements -- particularly with U.S. start-up firms -- to gain access to research results that would not otherwise be available to them. Policy issues, such as whether these agreements help or hinder the U.S. competitive position in biotechnology, remain controversial and unresolved.

Chapter 7

U.S. Industrial Research Collaborations in Biotechnology

Just as foreign firms will sign international collaborative research agreements in order to produce research results which would not otherwise be available to them, many companies within the U.S. enter into collaborative research agreements with each other for the same reason. While there are an undetermined number of such research agreements (as well as marketing and other types of agreements) involving all types and sizes of firms, the general pattern seems to be of large companies with no or little previous experience in biotechnology, entering into research agreements with smaller, start-up biotechnology firms (Kenney, 1986). In part, this is probably because it is less expensive and incurs less risk for the larger company than to begin in-house efforts de novo.

Those interviewed were asked what information they had concerning industry-industry collaboration in biotechnology, and it appears there currently exists no comprehensive, publicly available information on the topic. In part this is because of the intense secrecy and competition in the industry, but it is also due to the fact that this kind of information is seen as proprietary by biotechnology firms. Those that are publicly held corporations usually document their collaborative agreements with other industrial firms in their mandatory 10K filings. However, most of the new biotechnology ventures are privately held firms that are under no such requirements. It would seem that the only time one sees that kind of information is in the press releases and reports floated to the media just prior to a start-up firm going public with an IPO (initial public offering).

Gary Pisano, a graduate student at the University of California at Berkeley has been conducting dissertation research on this topic. Pisano reiterated that there currently exists no database on U.S. industry-industry research collaborations, although in conducting research for his thesis he is creating one. Pisano estimates that there are:

- About 800 biotechnology firms worldwide.
- Between 1000 and 1500 joint venture agreements among them -- although how many of these are strictly research collaborations is as yet unknown.
- Three quarters of the agreements are between large and small firms.
- Less than one quarter of the agreements are international collaborations.

His research to date suggests that big firms are mostly gaining licenses to market products through these agreements, but not licenses to the technology to manufacture products. He characterized most of the agreements as "complementary" -- "looking for the things that each partner can't do for itself". In contrast to many analysts who think that the trend towards such joint venture agreements are on the wane, Pisano sees their number increasing, or at least remaining level (Gary Pisano, personal communication).

Summary

In general, U.S. industry-industry research relationships in biotechnology typically occur in one-to-one agreements between large firms and small firms. Benefits for the large firms in such arrangements are primarily access to cutting edge research and highly trained scientists; smaller firms seem to be seeking near-term cash flow to bankroll their projected growth and access to

the very powerful marketing capabilities of large corporations for their products, once developed.

Chapter 8

Recommendations and Policy Issues

Serving the Public Interest: The Trade-off Problem

In the long-run, the trade-off made between the potential benefits that can accrue from university-industry research collaborations in biotechnology and the problems and risks that may be associated with such relationships, will depend on how the public and the policy-making community value the outcomes of these new partnerships. As Blumenthal, Gluck, Louis, Stoto, and Wise (1986) commented, the "long-term implications of current findings are hard to estimate". Nonetheless, they identified three trade-offs worth watching:

- Any losses to science or to university values that result from marginal increases in the level of secrecy in universities may be more than offset by net additions to knowledge that result from the infusion of industry funds into faculty laboratories.
- Marginal shifts in the direction of the university research agenda toward more applied and commercially relevant projects may have benefits for human health and economic growth that far outweigh the risks to scientific progress.
- In the long-run, the continued well-being of the universities and academic science depends to a significant extent on the public's perception that supporting university research contributes directly to practical results.

But university researchers are not the only ones concerned with the trade-offs. As Howard A. Schneiderman, Senior Vice President, R&D for Monsanto Co., and an important force behind that corporation's long-term research agreement in biotechnology at Washington University, said during Congressional Hearings in 1982:

> "I am confident that we not only have safeguarded the academic freedom of Washington University, but, in fact, we are enhancing it. We are as concerned as you that the academic enterprise be preserved. We are convinced that our contract not only preserves the goose that lays golden eggs, but will significantly increase its egg production for the public good" (Hearings, 1982, p. 25).

Others have said that it is truly in the national interest to develop new institutional arrangements that are potentially capable of reducing the time lag between advances made in the basic research laboratory and the application of those advances to human service (Donald Kennedy, as stated in Hearings, 1981). It would appear that the public interest is best served when the results of research are published and made available to the scientific community, and the academic work that is commercially valuable is patented and does in fact reach the marketplace faster through collaborations between the universities and the industrial community.

Making Collaborative Research Work

In the meantime, there are measures that can be taken to strengthen university-industry research relationships for all participants, and to maximize some of their potential benefits, while minimizing their problems and risks. The specific recommendations that follow are a synthesis of ideas taken from the literature review and interviews conducted during the course of this project:

- Universities and the industrial firms involved should ease the introduction of academic-business partnerships on campus with extensive prior discussion in which all relevant parties including students, faculty, university administrators, and corporate executives participate.

- Universities should negotiate collaborative agreements that are consistent with the values and missions of their institutions and should include as essential elements of any such agreement:
  - The scope of the agreement (e.g., particular research area(s) supported; time commitments of faculty participants).
  - Control over the conduct of the research (e.g., who selects areas of research, specific projects, and methodologies; provisions for internal and/or external advice and review).
  - Sponsor's responsibilities (e.g., funding; staff support; equipment; materials contributed).
  - Treatment of proprietary information.
  - Publication requirements (e.g., pre-publication review delays).
  - Patent rights and income (e.g., title retention; license agreements; term or life of the patent).
- Once established, universities should carefully monitor their collaborative research relationships with industry (at the university, not the departmental level) and rigorously enforce:
  - Disclosure rules -- the California standard was suggested as a norm.
  - Conflict of interest statutes.
  - Limitations on excessive outside consulting by faculty members.
  - Sanctions against faculty that retain "full-time" status at the university and are simultaneously executives in their own companies with "full-time" management responsibilities.
- Universities should contribute intellectual resources to collaborative research arrangements, not financial ones -- "the bounds can vary, but universities shouldn't be in the business of owning and running companies, that's the line."

Though some, like Kenney advocate a set of "national rules at the agency or congressional level" to dictate what is considered in and out of bounds for universities in their interactions with industry (a violation of the rules would mean a federal funding cut off for the university in question), it is difficult to see how monitoring university-industry research relationships is a legitimate federal role. Such things are clearly best done at a more local

level -- the university or the firm involved, or even the state economic development program that may be providing incentives to promote the partnership.

Who is better suited to police faculty members than university administrators? Who is more aware of the long-term risks of "polluting the ivory tower" with commercial interests than industrial leaders, many of whom are alumni of these same institutions? And what level of government is better situated to oversee the trade-offs between industrial and academic interests than the states that are struggling to preserve both kinds of indigenous resources within their geographic boundaries?

In short, there is no clear federal role that the government can or should play in monitoring such collaborative relationships, although the government's continued funding of the academic research that makes industry-university research arrangements attractive is essential. In addition, if one believes in the commercial potential that can result from university-industry research relationships, and their ultimate impact on America's capacity to compete technologically in global markets, there are federal and state roles to be played in the promotion of collaborative agreements.

NSF's University/Industry Cooperative Research Centers and Projects Programs (now unfortunately defunct) were examples of federal initiatives that were effective primarily because of the indirect brokering and catalytic role they played in matching university and industrial needs and resources. The effectiveness of NSF's more recent and greatly expanded Engineering Research

Center (ERC) Program has not yet been proven and several factors, including the heavy reliance in funding decisions on scientific merit alone in isolation of other potentially relevant award criteria, the inadequate coordination by federal officials with state programs and plans for related or even competing initiatives, and the lack of clearly defined evaluation and monitoring criteria for a program that will consume nearly $50 million in the FY 1988 budget, may impede the ERC's ultimate success.

Further Research Needs

Finally, these are a number of issues that were uncovered in the course of this project that warrant investigation and further research. These include:

- How do collaborative research arrangements in biotechnology differ by sector or area of research?
- Do foreign company research collaborations with U.S. universities and industrial firms help or hinder U.S. industrial competitiveness?
- What criteria should be used to measure the effectiveness of industry-university research relationships?
- Which collaborative research relationships are working? Can general principles (not rules) be developed to guide future program development that take into account the kind of situation, the size of the university, the industry in the state, the technological area, and the values of individual researchers?
- How have departmental cultures been affected by collaborative research arrangements and what are the impacts on students and post-doctoral fellows?
- How does the size of the collaborating industrial partner affect the benefits and problems resulting from university-industry research arrangements?
- Which hypothesis is more accurate -- "the more the more" or "the less the less"? Are faculty that are involved in collaborative research arrangements more productive overall, or is it a zero sum game?

Many more empirical studies are required and a great deal more experience with collaborative research relationships is needed before either the outcomes or the sides of the trade-off equation are adequately understood, and society can make an informed judgment.

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APPENDIX A

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2. Author:
   April Burke

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3. Author:
   Henry Etzkowitz

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4. Author:
   Lois Peters and Herbert I. Fusfeld

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5. Author:
   Martin Kenney

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6. Author:
   Sheldon Krimsky

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Leonard Minsky

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Kenneth P. Ruscio

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APPENDIX B

SOLOMON ASSOCIATES

February 23, 1987

MEMORANDUM TO THE FILES

From: Trudy S. Solomon

Subject: List of Interviewees and Schedule for OTA Study on "Collaborative Research Relationships in Biotechnology"

Interviewee	Schedule
1. David Blumenthal, M.D. Senior Vice President Brigham and Women's Hospital Corporation 75 Francis Street Boston, MA 02115 (617) 732-5696	Interview: March 4, 9 a.m.
2. Lois Peters, Ph.D. Center for Science and Technology Policy RPI Lallay Management Center Troy, NY 12180-3590 (518) 266-6836	Unavailable to be Interviewed
3. Martin Kenney, Ph.D. Assistant Professor Department of Agricultural Economics and Rural Sociology Ohio State University 2120 Fyffe Road Columbus, OH 43210-1099 (614) 292-6971	Interview: Feb. 26, 10 a.m.
4. Sheldon Krimsky, Ph.D. Department of Urban and Environmental Policy Tufts University Medford, MA 02155 (617) 381-3394	Interview: Feb. 25, 3:30 p.m.

Suite 550
4520 East-West Highway
Bethesda, MD 20814
301/986-0466

5. Richard Nelson, Ph.D.
School of International
and Public Affairs
Columbia University
New York, NY 10027
(212) 280-8720

Interview: Feb. 27, 3 p.m.

6. Steven H. Holtzman
Vice-President
Embryogen
Innovation Center
One President Street
Athens, Ohio 45701
(614) 593-1617

Interview: Feb. 26, 2 p.m.

7. Dr. Gilbert S. Omenn
Dean
School of Public Health
Mail Stop SC-30
University of Washington
Seattle, Washington 98195
(206) 543-1144

Interview: March 10, 7 a.m.

APPENDIX C

SOLOMON ASSOCIATES

February 23, 1987

Interviewee: _____

Date/time contacted: _____

INTERVIEW GUIDE

COLLABORATIVE RESEARCH RELATIONSHIPS IN BIOTECHNOLOGY

This is Dr. Trudy Solomon calling from SOLOMON ASSOCIATES -- a Washington, D.C. based consulting firm. We have been funded by the Congressional Office of Technology Assessment (OTA) for a study of issues related to collaborative research arrangements in biotechnology. The primary focus is on industry-university collaboration.

The study is being conducted in two phases. The first phase consists of a review of current research on the structure and possible effects of collaborative research in biotechnology. The second consists of a series of in-depth interviews with primary investigators who have conducted research or written publications in this area. Since your work in this area:

_____

_____

was reviewed during the first phase of this study, you were one of the people selected by OTA to be interviewed in phase two. The information is to be used in the OTA assessment of "U.S. Investment in Biotechnology".

We will be asking both general questions about collaborative research in biotechnology, and specific questions about your own conclusions and findings in this area. The interview will take about an hour to complete.

Would you be willing to participate? _____

What would be a good time for you this week to schedule the interview?

_____

Thank you. I will talk with you then.

Suite 550
4520 East-West Highway
Bethesda, MD 20814
301/986-0466

INTERVIEW GUIDE

COLLABORATIVE RESEARCH RELATIONSHIPS IN BIOTECHNOLOGY

Study Background

I would like to begin the interview by asking you some general questions about collaborative research arrangements in biotechnology. Using OTA's terminology, the term "collaborative" includes: institutional-institutional arrangements (such as those between a university and a corporation or firm, or those between a number of industrial partners and one or more universities -- often with state or federal involvement) and individual-institutional arrangements (such as those between an academic scientist and a biotechnology company). OTA is also interested in industry-industry relationships, to the extent that they exist in biotechnology.

The literature on university-industry research arrangements in biotechnology discusses two vastly different and opposing viewpoints on the problems, benefits, and potential outcomes of collaboration. In the extreme, I would state these rhetorical views as follows:

- The Negative View: That the influx of commercial interests on campus has perverted the fundamental values and structure of universities, distorted the research agenda, and adversely affected everything from academic freedom and scientific communication to basic professorial responsibilities, including the teaching and training of students.

- The Positive View: That university-industry research collaboration is the critical key to enhancing our nation's industrial competitiveness, productivity, and innovation, and that such arrangements will facilitate critically needed technology transfer and result in sustained economic development, job retention, and job creation.

Many assumptions are made on both sides of the issue, and often the only evidence offered to back these up is anecdotal data, not hard facts. Since one of OTA's primary objectives in this study is to assess the validity of these opposing views, please provide evidence and data to substantiate your opinions whenever possible.

General Questions (to be asked of all interviewees)

1.A. What factors have made collaborative research in biotechnology so attractive to universities, industry, and individual scientists?

1.B. Do you expect this trend toward university-industry collaboration in biotechnology to continue? Why, or why not?

2. What do you think are the major benefits of research collaboration in biotechnology?

   A. For Universities?

   B. For Industry?

   C. For Individual Scientists/Professors?

   D. For Students?

   E. For U.S. Industrial Competitiveness?

3. What do you think are the major problems of research collaboration in biotechnology?

   A. For Universities?

   B. For Industry?

   C. For Individual Scientists/Professors?

   D. For Students?

   E. For U.S. Industrial Competitiveness?

4. Do the benefits and problems you have identified vary by type of collaborative arrangement (e.g., I/U Centers or Consortium; long-term I/U contracts; consulting; "entrepreneurial scientists")? If so, how?

5. Do the benefits and problems you have identified vary by sector or area of research (e.g., agriculture; chemicals; pharmaceuticals)? If so, how?

6. Do the benefits and problems you have identified vary by size or nationality of the collaborating industrial partner (e.g., small entrepreneurial venture; large corporation; foreign company)?

7.A. How are collaborative research arrangements in biotechnology similar to, or different than, such arrangements in other fields?

7.B. What "lessons learned" can be identified from collaborative research arrangements in other applied fields that can guide program development in biotechnology?

8. What specific recommendations do you have for improving the process or the outcome of collaborative research in biotechnology?

9. What (if any) information do you have concerning industry-industry collaboration in biotechnology?

10. What (if any) information do you have concerning collaborations between foreign companies and U.S. universities, or U.S. academic researchers, in biotechnology?

Before turning to some specific questions about your own research findings and conclusions in this area, is there anything else of a general nature you feel is pertinent to collaborative arrangements in biotechnology, that we haven't discussed?

APPENDIX D

A Typology of Research Interactions

General Research Support	Cooperative Research Support	Knowledge Transfer	Formal Technology Transfer
A. Institutional Gifts in Support of Research 1. Monetary Gifts 2. Equipment Donation 3. Contributions for Research Facilities	A. Institutional Agreements 1. Contract Research 2. Equip. Transfer & Loans 3. Grants to a Professor 4. Graduate Fellowships Support 5. Gov't. Funded U/I Cooperative Research	A. Personal Interactions 1. Personnel Exchanges 2. Mechanisms for Personal Interactions: Advisory Boards Seminars, Speakers Programs, Publication Exchange 3. Adjunct Professorships 4. Consulting	A. Product Development and Modification Programs 1. Extension Services 2. Innovation Centers
B. Endowment/Annuity/Trust Funds 1. Research Facilities 2. Endowment Chair	B. Group Arrangements 1. Special Purpose Industry Affiliate Programs (Focused & Discipline Programs) 2. Research Consortia	B. Institutional programs 1. Institutional Consulting 2. General Industry Associates Programs	B. Univ. and/or Industry Associated Institutions & Activities Serving an Interface and/or Foundation for U/I Research Interactions 1. U/I Research Coop. & Technology Brokering & Licensing Activities 2. University Connected Research Institutes 3. Industrial Parks 4. Spin-Off Companies & U/I Research
	C. Institutional Facilities 1. Coop. Research Centers 2. Univ.-Based Institutes Serving Industrial Needs 3. Jointly Owned or Operated Facilities & Equipment	C. U/I Cooperation & Educ. 1. Univ. Serves as Source of Graduates for Industry: Internships, U/I Coop. Training Programs 2. U/I Coop. in graduate curriculum development; Alumni Initiation of Research Interactions 3. Continuing Education is Utilized to Initiate Research Collaboration: Short Courses, Personal Contacts 4. Industry-Funded Fellowships	
	D. Informal Cooperative Interaction: Co-Authored Papers, Equipment Sharing	D. Collective Industrial Interactions 1. Trade Associations 2. Ind. Educ. Affil. 3. Ind. Sponsored R&D Org. 4. Ind. Res. Consortia	

Source: Peters and Fusfeld (1981), p. 68.

APPENDIX E

Major Biotechnology Centers or Programs at Universities*

University	Date established	Funding ($ million)	Sources of funds	Building	Colleges involved	Special comments
Univ. California, Berkeley, and Stanford (through Engenics)	1981	10.0	Bendix General Foods Koppers Mead Noranda Mines Elf Aquitaine	No	Engineering, medical school	A research consortium funded by companies
Univ. California, Berkeley Plant Gene Expression Laboratory	1984	8.0	USDA, private, university	Yes	Agriculture, engineering	Plant gene expression
Cornell University Biotechnology Institute	1983	7.5	General Foods Union Carbide Eastman Kodak State government University	Planned	All colleges	State of New York has provided $2 million in funding and an additional $18 million is pending
Univ. of Illinois Center in Crop Molecular Genetics	1983	2.0	Sohio Co.	No	Agriculture	Funded solely by Sohio
Biotechnology Center	1984	None yet	None yet	No	All colleges	The center will be organized as industrial associate program
Univ. of Michigan Center for Molecular Genetics	1982	8.0	Howard Hughes Medical Institute Salsbury Laboratory	Yes	Medical	
Michigan State Univ. Biotechnology Center	1983	6.0	State legislature Kellogg Foundation	Planned	All colleges	Connected with private company, Neogen
New Mexico State Center for Semi-Arid Plant Biotechnology	1984	7.0	State legislature	Planned	Agriculture	Only area of research is desert plants
Rutgers Univ.	1985	34.0	Bond issue	Yes	Agriculture, medical school	One center for agriculture and one for medicine

*This table is not exhaustive

Source: Kenney (1986), pp. 44-45.

APPENDIX F

Summary of Large University-Industry Research Grants*

Year	University	Company	Amount ($ million)	Duration (years)	Investigator	Area of research
1974	Harvard Medical School	Monsanto	23.5	12	M. Folkman B. Vallee	Cancer tumors
1980	MIT	Exxon	8.0	10	J. Longwell P. Sarofim	Combustion
1981	Massachusetts General Hospital	Hoechst	70.0	10	H. Goodman	Genetics
1981	Harvard Medical School	Du Pont	6.0	5	P. Leder	Genetics
1981	UC Davis	Allied	2.5	3	R. Valentine	Nitrogen fixation
1981	Scripps Clinic & Research Foundation	Johnson & Johnson	30.0	—	—	Synthetic vaccines
1981	Washington Univ.	Mallinkrodt	3.8	5	J. Davie	Hybridomas
1981	Yale	Celanese	1.1	3	N. Ornston	Enzymes
1982	Johns Hopkins	Johnson & Johnson	1.0	—	—	Biology
1982	Rockefeller Univ.	Monsanto	4.0	5	N. Chua	Photosynthesis
1982	Washington Univ.	Monsanto	23.5	5	—	Biomedical
1982	MIT	W. R. Grace	8.0	5	P. Thilly	Amino acids
1982	Yale	Bristol-Myers	3.0	5	—	Anticancer drugs
1982	Cold Spring Harbor	Exxon	7.5	5	—	Molecular genetics
1983	Rochester	Kodak	0.45	—	—	DNA
1983	Medical Univ. South Carolina	Chugai	0.5	3	A. Streikauskas	Monoclonal antibodies
1983	Univ. of Illinois	Sohio	2.0	5	—	Plant molecular genetics
1983	Columbia	Bristol-Myers	2.3	6	A. Efstratiadis	Gene structure
All years a number of large grants by Agrigenetics to various researchers at a number of universities						

*Because of the secretive nature of many universities, these data are tentative and incomplete.

Source: Kenney (1986), p. 56.

APPENDIX G

THE RESOURCE CENTER

DIVISION OF ECKHART AND COMPANY, INC.

SUITE 550
4520 EAST-WEST HWY.
BETHESDA, MD 20814
(301) 652-0106

TO: Trudy Solomon

FROM: Dona Mennella

DATE: February 25, 1987

SUBJECT: Biotechnology Search

Presented below are the search strategy, list of databases, and findings from your request for source material and documentation of foreign company research collaborations with U.S. universities in biotechnology.

Search Strategy

The following terms were searched:

First set - Foreign or Japan(ese) or Europe(an) or Switzerland or United Kingdom or Britain or France

Second set - Invest(ment, or) or Participation or Collaboration

Third set - College(s) or Universit(y, ies) or Academi(c, a) or Professor(s)

For those databases not dealing primarily with biotechnology, the term "Biotech(nology)" was added to the three sets above.

Databases

NEXIS - Newspaper File (American Banker, BBC Summary of World Broadcasts, The Bond Buyer, The Current Digest of the Soviet Press, Computerworld, The Christian Science Monitor, DM News, Facts on File World News Digest, Financial Times, InfoWorld, The Japan Economic Journal, Legal Times, The MacNeil/Lehrer News Hour, Manchester Guardian Weekly, The National Law Journal, The New York Times, Worldpaper, The Washington Post) and the journals Bioprocessing Technology and Genetic Technology News.

DIALOG - Telegen database, covering genetic engineering and biotechnology from 5,000 worldwide sources including journals, conferences, corporate and government reports, and independent laboratory reports.

Findings

As we discussed, the information exists on academic-industrial relationships, but only on an intra-country basis.